PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	03.02.2005
Applicant's or agent's file reference: P071899WO	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/04532	20.10.2003	22.10.2002

Applicant: THE MEDICAL HOUSE PLC et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P071899WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/04532	International filing date *(day/month/year)* 20.10.2003	Priority date *(day/month/year)* 22.10.2002
International Patent Classification (IPC) or both national classification and IPC A61M5/30		
Applicant THE MEDICAL HOUSE PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.05.2004	03.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tlx 523656 epmu d Fax +49 89 2399 - 4465	Authorized Officer Krassow, H Telephone No. +49 89 2399-2096

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/04532

I. Basis of the report

1. With regard to the elements of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1, 3-26	as originally filed
2	filed with telefax on 19.01.2005

Claims, Numbers

1-22	filed with telefax on 19.01.2005

Drawings, Sheets

1/28-28/28	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT International application No. PCT/GB 03/04532

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 21

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 21

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT International application No. PCT/GB 03/04532

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-7,13-18,22 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7,13-18
	No:	Claims	22
Inventive step (IS)	Yes:	Claims	15-18
	No:	Claims	1-7,13,14,22
Industrial applicability (IA)	Yes:	Claims	1-7,13-18,22
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 21 seeks to define the subject-matter to be protected by reference to the figures instead of by technical features.

Re Item IV

Lack of unity of invention

1. This application is deemed to comprise multiple groups of inventions, therefore it does **not meet the requirements for unity of invention**, as set forth in Rule 13.1 PCT. The separate groups of inventions are considered to be:

I) **Claims 1-7, 13-18 and 22** essentially define a needleless injection device comprising
1) a medicament cylinder with a sliding piston therein,
2) a ram to drive the piston and an energy accumulator to drive the ram,
3) the rear end of the ram extending into a discharge assembly,
4) the discharge assembly having a retention member having a plurality of retention elements radial displacement of which is prevented by a release ring to prevent discharge of the ram, and
5) the retention elements being integral with the retention member, and each having an enlarged head which can move into and out of engagement with a groove on the ram by deformation of the material of the retention member, wherein
6) the retention member comprises a collet with radially spreadable fingers and the release ring having a collet lock sleeve which limits outward radial movement of the collet fingers (cf. claims 2-4).

II) **Claims 8-12** essentially define a needleless injection device comprising
1) a medicament cylinder with a sliding piston therein,
2) a ram to drive the piston and an energy accumulator to drive the ram,
3) the rear end of the ram extending into a discharge assembly,
4) the discharge assembly having a retention member having a plurality of retention elements radial displacement of which is prevented by a release ring to prevent

discharge of the ram, and

5) the retention elements being integral with the retention member, and each having an enlarged head which can move into and out of engagement with a groove on the ram by deformation of the material of the retention member, with further

6) the device comprising a nozzle-lock assembly (claim 8).

III) **Claims 19 and 20** essentially define a needleless injection device comprising

1) a medicament cylinder with a sliding piston therein,

2) a ram to drive the piston and an energy accumulator to drive the ram,

3) the rear end of the ram extending into a discharge assembly,

4) the discharge assembly having a retention member having a plurality of retention elements radial displacement of which is prevented by a release ring to prevent discharge of the ram, and

5) the retention elements being integral with the retention member, and each having an enlarged head which can move into and out of engagement with a groove on the ram by deformation of the material of the retention member, and

6) the energy accumulator being a spring in a variable volume chamber (claim 19).

Feature 6) of group I) addresses the objective technical problem of providing a means to prevent the flexible fingers to move out of engagement with the ram, thus to prevent axial movement thereof (description, p. 19, l. 27 - p. 20, l. 4).
Feature 6) of group II) addresses the objective technical problem of providing a releasable means for locking a nozzle to the device (description, p. 11, l. 32 - p. 12, l. 6).
The last feature of group III) address the objective technical problem of providing a needleless injector with an integral firing force adjustment means (cf. functional feature of claim 19).
The **only technical features common** to any combination of the various groups of claims are, **at most**, features 1)-5). These features are already known in combination from the prior art, cf. e.g. WO 02 47746 A.
Therefore the requirement of unity is not fulfilled, according to Rule 13.2 PCT, because there are **no common special technical features.**

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

INTERNATIONAL PRELIMINARY EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/GB 03/04532

Reference is made to the following documents:

D1: US 6 099 503 (STRADELLA GIUSEPPE) 8 August 2000 (2000-08-08), **not cited in the search report**

D2: WO 02/47746 A (AAMARK MIKAEL ;BERGENS THOMAS (SE); SHL MEDICAL AB (SE)) 20 June 2002 (2002-06-20)

D3: WO 03/070296 A (LESCH PAUL R JR ;ANTARES PHARMA INC (US)) 28 August 2003 (2003-08-28)

1. The subject-matter of **claim 1 is not inventive** (Article 33(3) PCT).

1.1 Document D1 is considered as the most relevant prior art.

D1 discloses an injection device comprising a medicament cylinder (3) having an injection nozzle (needle (4)), and a piston slidingly received in the cylinder to drive the medicament through the nozzle. The piston is driven by a ram (piston (21)), which is driven by an energy accumulator (compression spring (22)) when discharged, which is disposed between the ram and a discharge assembly (cylinder (23)+resilient tabs (19)), wherein the rear end of the ram extends into the discharge assembly. In particular, as shown in **Figures 13 and 14**, the discharge assembly also comprises a retention member (resilient tabs (19)) fixed in the assembly, which has a plurality of retention elements (lugs (20)) spaced around and adapted to locate on the ram when in a charged position. There is further a release ring (control sleeve (17)) surrounding the retention elements to prevent their radial outward displacement and discharge of the ram. Discharge of the ram is caused by axial displacement of the release ring, whereby the retention elements are released (cf. col. 7, l. 1-22). The retention elements are integral with the retention member, and have an enlarged head which can move into and out of engagement with a recess (21a) on the ram by deformation of the material of said retention member.

The fact that the subject-matter of claim 1 differs therefrom in that it is a needleless injection device does not involve an inventive step. Whether an injection device is needleless or not is of minor importance as far as the triggering of the injection process is concerned, which in the present case is the technical problem the subject-matter of claim 1 is directed to.

1.2 The subject-matter of claim 1 also appears to be not inventive with respect to D2.

Document D2 discloses an injection device (cf. Fig. 7), wherein a plurality of retention elements (60) are in engagement with a recess on ram (76) by means of release ring (46).

In D2, the discharge of the ram is caused by axial displacement of retention elements

(60) caused by the user pressing button (54), instead of axial displacement of release ring (46) as defined in present claim 1. This solution, however, is regarded as a mechanical and technical equivalence, as it is the relative movement between a release ring and the retention elements which causes the triggering. The skilled person is readily aware of both possibilities and one solution is a mere matter of normal design alternative over the other.

1.3 The applicant's argumentation, the skilled man would not have considered auto-injectors, i.e. injection devices comprising a needle, as shown in D1 and D2 is not convincing. Although it is agreed that the forces required to inject medicaments in the case of a needleless injector are much higher, the working principle of the triggering mechanisms are the same in both cases. Particular components of any injector, whether auto-injector or needleless injector, always have to be designed and dimensioned according to the particular forces present in a particular injector. The skilled person, which is the same for both, auto-injectors and needleless injectors, is well aware of that and would not have automatically disregarded the well known discharge assembly solutions present in auto-injectors.
Further, with respect to applicant's argumentation regarding D1, it is to be noted that the discharge assembly (23) in fact comprises a retention member (19), the rear end (52) of the ram (21) extends into said discharge assembly, and the energy accumulator (22) is disposed between the ram and the discharge assembly. Thus, there are no constructional differences as argued by the applicant.

2. The additional features of claims 2-7, do not appear to render the subject-matter of any claim to which said claims refer inventive (Article 33(3) PCT). These features are either already disclosed in D1 or D2, or represent mere matter of normal design alternatives the skilled person is readily aware of.
Claims 2-7: D1: the retention member comprises a collet (19) the radially spreadable fingers spread radially outwards and out of engagement with the ram (21). The fingers are also biased radially inwardly (by control sleeve (17)), and their outward radial movement is limited by a collet lock sleeve (control sleeve (17)), which axial displacement is limited by the collet fingers (cf. col. 12, l. 52-55). Although the collet fingers (20) are provided with tapered surfaces, the tapered surfaces as defined in claim 6 do not appear to solve any objective technical problem anyway,

and there is a compression spring (22).
These arguments also apply to D2.

Claims 13, 14: D1: the axial displacement is provided by the resistive-sensitive trigger-shroud (tube (5), cf. col. 7, l. 6-22) to be pressed against the patient's skin. Cf. also D2, Fig. 6. Safety locks for avoiding unwanted firing of an injector are general features known to the skilled man and, as such, not inventive.

3. The subject-matter of claims 15-18 appears to fulfil the requirements of the PCT with regard to Article 33(2)-(4) PCT.

3.1 An axially extending tab in combination with the features of claims 14, 13 and 1, defines an injection device wherein unintentional firing of the device is prevented, by a tab serving as an end stop, which in the locked position, prevents axial movement of the shroud.
Such a solution is not rendered obvious by the prior art at hand.

3.2 The definition given in claim 15, as such, however, is unclear (Article 6 PCT). A possible amended claim 1 directed to the subject matter of present claim 15 should make clear how the safety lock is intended to work in the sense of lines 16-25 of page 21 of the description. Otherwise the skilled person is unable to imagine the working principle of the safety lock.

4. The subject-matter of independent claim 22 is not novel (Article 33(2) PCT).
A discharge assembly having all the features of claim 22 is known from D1, Figures 13 and 14, cf. the reasoning given above under 1.1.

Further comments:

1. Independent claim 1 should have been cast in the **two-part form** (Rule 6.3(b) PCT) with the preamble containing those features known in combination from the closest prior art (**D1**) (Rule 6.3(b)(i) PCT).

Re Item VI

Certain documents cited

INTERNATIONAL PRELIMINARY EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/GB 03/04532

Document D3 was published after the priority date but before the filing date of the present application. Its disclosure, in particular with regard to the discharge assembly (cf. p. 10, l. 8-18) appears to be particularly relevant and could be used in a future Regional Phase with respect to novelty.

delivers the medicament by expelling it rapidly through a small aperture in the nozzle so that the medicament passes through the patient's skin.

The delivery of a medicament using a needleless injector is typically much less traumatic than using a conventional syringe with a needle. This is because the nozzle aperture is usually of smaller diameter than a hypodermic needle and secondly because the medicament is delivered more rapidly using a needleless injector than by using a needle.

Conventional injectors of the type described above have a relatively noisy operation owing to the use of ball bearings in the discharge mechanism. The discharge mechanism of US5,782,802 is described therein with reference to Figure 1 (see column 5, line 39 - column 6 line 22). In particular, ball bearings 48 are trapped between the ram's rear neck 36 and the inner front end of the bushing 44. In this position, the ball bearings 48 lock the ram 34 to the discharge mechanism 32. In order to discharge the device, the bushing 44 has to move forward allowing ball bearings 48 to move outward, away from the ram's neck 36, which consequently allows the ram's rear shoulder 38 to pass through, pushed vigorously by the fully compressed main spring 22.

The movement of the ball bearings 48 is only limited by the confines of the relevant parts of the device in which they are located. It is possible that the ball bearings will "rattle" within those confines, especially given the great force stored in the fully compressed main spring which is suddenly released upon discharge of the device,

CLAIMS

1. A needleless injection device comprising

a cylinder for medicament having an injection nozzle at a forward end thereof and an opening at its rearward end;

a piston sliding in the cylinder through said open end, in use, to drive the medicament through the nozzle;

a ram to drive the piston into the cylinder and having a longitudinal axis; and

an energy accumulator to drive the ram when discharged and disposed between the ram and a discharge assembly, a rear end of the ram extending into said discharge assembly; wherein

the discharge assembly comprises a retention member fixed in the assembly, said retention member having a plurality of retention elements spaced around and adapted to locate on the ram when in a charged position of the ram, and a release ring surrounding said retention elements to prevent radial outward displacement thereof and discharge of the ram; and wherein

axial displacement of said release ring releases said retention elements and causes discharge of the ram by said accumulator;

characterised in that said retention elements are integral with said retention member and each has an enlarged head which can move into and out of engagement with a groove or recess on the ram by deformation of the material of said retention member.

2. A device as claimed in claim 1 wherein said

retention member comprises a collet having radially-spreadable fingers, which collet in use moves between said first position in which said fingers engage with said ram and said second position in which said fingers spread radially out of engagement with said ram.

3. A device as claimed in claim 2 wherein said collet fingers are biassed radially-inwardly.

4. A device as claimed in claim 2 or claim 3 wherein said release ring comprises a collet lock sleeve which limits outward radial movement of said collet fingers.

5. A device as claimed in claim 4 wherein axial movement of said collet lock sleeve is limited by abutment thereof against said collet fingers.

6. A device as claimed in claim 4 or claim 5 wherein said collet lock sleeve and said collet fingers are respectively provided with cooperating tapered surfaces.

7. A device as claimed in any of the preceding claims wherein said energy accumulator is a compression spring.

8. A device as claimed in any of the preceding claims further comprising a nozzle lock assembly which enables a nozzle to be releasably attached to said device upon insertion of a nozzle into an end thereof, the nozzle lock assembly including

on one of said nozzle or said end of the injection device, a twist cap containing a moveable spacer which has a non-circular aperture therethrough; and

on the other of said nozzle or said end of the injection device a protrusion having a correspondingly shaped non-circular outer surface which, if aligned therewith, can pass through said non-circular aperture,

wherein, upon twisting of said twist cap, the moveable spacer twists with respect to said protrusion so that the non-circular aperture of the spacer can be selectively brought into and out of alignment with the non-circular outer surface of said protrusion, so that said protrusion is respectively either free to move in or out of said aperture or is trapped therein by said moveable spacer.

9. A nozzle lock assembly as claimed in claim 8 wherein said twist cap is located on said end of the injection device and said protrusion is located on said nozzle.

10. A nozzle lock assembly as claimed in claim 8 or claim 9 further comprising a second protrusion having the same non-circular outer surface and being axially spaced from the first protrusion.

11. A nozzle lock assembly as claimed in any of claims 8 to 10 wherein said non-circular aperture and said non-circular outer surface are substantially triangular.

12. A nozzle lock assembly as claimed in any of claims 8 to 11 further comprising a mark on said twist cap which indicates the relative alignment of the non-circular aperture and the protrusion.

13. A needleless injection device as claimed in any of the preceding claims characterised in that said axial displacement is provided by means of a resistance-sensitive trigger comprising an axially-moveable shroud forming at least part of the outer surface of said device, the trigger being activated by application of forward axial force to the shroud which is resisted by the skin of the patient at an injection site.

14. An injection device as claimed in claim 13 wherein said resistance-sensitive trigger further comprises a safety-lock, moveable between a locked position, in which the device cannot be discharged and an unlocked position in which the device can be discharged.

15. A injection device as claimed in claim 14 wherein said safety lock comprises at least one axially-extending tab which serves as an endstop which, in said locked position, prevents axial movement of said shroud.

16. An injection device as claimed in claim 15 wherein said tab is driveable between said locked and said unlocked positions by a rotatable drive plate actuated by a switch.

17. An injection device as claimed in any of claims 14-16 wherein, in said unlocked position, said tab moves axially rearward to engage in a recess in an endcap of the injection device.

18. An injection device as claimed in claim 17 wherein said tab is rearwardly biassed by means of a spring.

19. An injection, device as claimed in any of the preceding claims wherein said energy accumulator is a spring confined within a variable-volume chamber, the injection device further comprising an integral firing force adjustment mechanism which, in use, varies the volume of said chamber, effected by rotation of said ram.

20. An injection device as claimed in claim 19 wherein the rotation of the ram is effected by the turning of a key inserted through one end of said device.

21. A needleless injection device substantially as described herein with reference to any appropriate combination of the accompanying drawings.

22. A discharge assembly, suitable for use in a needleless injection device as claimed in any of the preceding claims, comprising a retention member fixed in the assembly, said retention member having a plurality of retention elements spaced around and adapted to locate on a ram when in a charged position of the ram, and a release ring surrounding said retention elements to prevent radial outward

displacement thereof and discharge of the ram; and wherein

axial displacement of said retention ring releases said retention elements and causes discharge of the ram by an energy accumulator;

characterised in that said retention elements are integral with said retention member and each has an enlarged head which can move into and out of engagement with a groove or recess on said ram by deformation of the material of said retention member.